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EEG INDICES IN CHILDREN WITH PRIMARY HEADACHE DISORDERS

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Both episodic migraine and tension-type headache (TTH) are characterized by attacks of strong headache. There is growing evidence that the brain functions are abnormal even within between-attack periods. We tried to evaluate interictal brain functions in children with primary headache using quantitative EEG. Sixty patients were recruited, 25 children with migraine and 35 with TTH. Patients were classified according to the ICHD. Migraine patients had significantly higher relative spectral powers of slow-wave bands (theta and delta) and decreased alpha relative powers in most of the regions examined than those in TTH patients. Apart from the above-mentioned specificities and negative correlation of age with the powers of delta and theta bands in both groups, we could not find other clinical variables that appeared to significantly affect EEG indices. Our results support that interictal brain dysfunction is, in general, more typical of migraine patients. These results shall help to contribute to better management and brain protection in children with headache.

Keywords: migraine, tension-type headache, children, interictal periods, quantitative electroencephalography, spectral power.

INTRODUCTION

Primary headaches are associated with significant functional impairment in social and work activities. These disorders in children are responsible for a number of lost school days [1]. Is there a link between epilepsy and migraine, is an obviously urgent question. A possible link between partial childhood epilepsy and migraine was assumed [2]. Migraine-like symptoms, such as visual disturbance, headache, and vomiting, occur in epilepsy and can be misdiagnosed as migraine [3]. Both conditions may coexist in some patients [4]. Neurophysiological methods showed evidence of altered cortical excitability in migraine patients [5–7]. Slow waves, with depression of background activity, were recorded during visual aura of migraine [8]. Interictal focal slow-wave and spike activities were also reported in children with migraine, suggesting a possible genetic link to focal childhood epilepsy [9].

Migraine is thought to be a progressing brain disorder that is associated with an increased risk of cognitive impairment [10]. Much less is known on the pathophysiology of tension-type headache (TTH) [11]. Migraine and TTH were thought to be associated with early pathologic changes in the brain and to share common pathogenic pathways [12]. The value of electroencephalography (EEG) in the diagnostics of patients with headache is at present controversial. EEG is not useful in routine evaluation of patients with headache, but it is useful when a possible seizure disorder is suspected [13]. However; EEG can be helpful in understanding the pathophysiology of headache and its effect on the developing brain. EEG can be objectively quantified by quantitative frequency analysis of EEG (QEEG) [14]. This technique has been used in migraine, but with inconsistent results [15, 16]. This may, in part, be due to inclusion of both preictal and postictal recordings in the analysis [17]. Up to 80% of children with migraine accompanied with aura demonstrated abnormal EEGs during headache [18]. Tension-type headache is also common in children [19] Both childhood migraine and childhood TTH may be associated with a cognitive deficit, which may indicate an associated brain damage [10, 20]. Ictal and interictal EEG abnormalities were found to be more common in migraine patients than in TTH patients [21]. Tension-type headache is much less investigated using interictal QEEG.

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The aim of our study was to explore and compare interictal brain functioning using QEEG in children with migraine and TTH.

METHODS

The study was conducted on 60 patients with primary episodic headache. Migraine or TTH was differentially diagnosed according to the International Classification of Headache Disorders, ICHD [22]. Thirty-one girls and 29 boys/teens, their ages ranged between 5 and 19 years, with a mean age of 14 ± 4.2 years, were involved in the study. They were consecutively recruited from the General Pediatric Outpatient Clinic in the Abuelresh hospital, Cairo University. All available medical files of patients were reviewed. Through-history taking and neurological examination were done for all patients. Brain imaging and laboratory investigation were also done, to exclude secondary headaches. Digital EEG was recorded from all patients (interictal blinded-off medications or stopped medications a day before), using Schwarzer BrainLaB 4 GmbH (Germany). The records were performed at the Clinical Neurophysiology unit of the Kasr El-Aini hospital. QEEG was done for all patients, for about 1 hour with 3-min-long hyperventilation and intermittent photic stimulation (IPS) episodes. Six epochs were selected for QEEG; three of them were during IPS provocation. The absolute and relative (normalized) spectral powers in records by 19 electrodes (Fp1, Fp2, F7, F8, F3, F4, C3,C4, T3, T4, T5, T6, P3, P4, O1, O2, Fz, Cz, and Pz) were studied in the following frequency bands, delta (1–3 Hz), theta (4–7 Hz), alpha (8–11 Hz), beta1 (12–15 Hz), and beta 2 (16–20 Hz). The relative powers were calculated as percentages of the power in a given frequency band compared with the total spectrum.

Statistical Methods. Data were statistically described in the following terms: mean ± s.d., median, frequencies (number of cases), and relative frequencies (percentages) when appropriate. Results were tabulated and statistically analyzed using statistical package SPSS ver. 16. Descriptive statistics were used. The unpaired Student *t*-test was used for the comparisons between two groups of quantitative variables. The difference between parameters was considered statistically significant at probabilities of the zero hypothesis below or equal to 0.05 [23].

RESULTS

Twenty-five patients (13 girls and 12 boys) had migraine headache. Their age ranged between 7 and 19 years, with the mean age of 14.8 ± 3.8 years. Thirty-five patients (19 girls and 16 boys) suffered from TTH. Their age ranged between 5 and 19 years, with the mean age of 13.0 ± 4.5 years. Of the migraineurs, 15 subjects had migraine with aura, while 11 did not experience any aura. Table 1 summarizes clinical criteria of the studied population.

The age demonstrated significant negative correlation with the absolute delta- and theta-band powers, with and without photic stimulation in both groups. Compared to TTH patients, migraine patients consistently had significantly greater relative powers of the slow-wave bands (theta and delta) in most of the studied regions, in baseline EEGs and even in further more regions during photic stimulation. There were significantly lower alpha relative spectral powers among migraine patients (Table 2). Clinical variables of the site of headache, duration, and frequency of attacks did not display consistent slow-waveband expression in QEEG readings.

DISCUSSION

Some EEG abnormalities, as increased alpha-wave variability and/or asymmetry, were reported in interictal recordings of migraineurs [24–26]. In our study, we found increased slow-wave spectral powers in interictal QEEGs of migraineurs compared to those patients with TTH. This is contestant with the data of other studies that evaluated interictal QEEGs in primary headache patients. In these studies, migraineurs showed increased focal slowing [26], greater slow-wave activity, and/or decreased alpha-wave activities [27, 28]. There were also an increased theta/alpha ratio [29] and a higher theta power [30, 31]. Slowing of the mean EEG frequency without significant changes in absolute powers was also observed during migraine attacks [32]. In children during visual aura, depression of alpha oscillations was recorded, followed by bifrontal and parieto-occipital increases in the delta power [27].

Our sampling was not suitable to extract certain epidemiological data. However, the ratio of migraine headache to TTH in our groups was somewhat higher than that reported in literature. At the same time, TTH was the predominant primary headache disorder in our sample, and it was more common in females, compared with the literature data. This can be attributed to the fact that our sampling was recruited from a tertiary center. Bugdayci et al. [33] found that TTH was the most common primary headache disorder, and it can be followed by migraine. Schwartz et al. [34] also found that TTH was more common in females in the age group between 18 and 29 years. Wong et al. [35] reported that TTH was 2–3 times more frequent than migraine among patients between 15 and 24 years old. Migraine patients had more frequent positive family history compared to TTH patients, but the difference was not statistically significant. Migraine has strong genetic basis [36–38]. Reports of familial occurrence of TTH, however, also do exist [39].

In our patients, migraine headache attacks were, most frequently, pulsating. Those were likely to be more severe and associated with nausea, vomiting, and photophobia, compared to TTH. Worsening of physical activity was significantly more common in migraineurs. These all were the criteria of migraine diagnosis, but this can be both the cause and the effect [40]. The duration of a headache episode in most cases is smaller than 6 hours, and this is comparable with the data of Linet et al. [41] who found that the average duration of the headache attack was 5.9 hours for males and 8.2 hours for females. Malik et al. [42] also found that the average duration of primary headache disorders was about 6.3 hours. It was acknowledged in some studies that migraine attacks can be shorter in children [43, 44]. We found that physical activity was the main precipitating factor for TTH, while fasting and sleep deprivation were the main such factors for migraine headache. This is consistent with Shah and Nafee [45], who found that stress and handicraft professions are the main predisposing factors for tension and cervicogenic headaches, while fasting is the primary precipitating factor for migraine. We found a significant negative correlation between the slow-wave power and age in both groups. A similar finding has been also reported in normal children [46].

Our study showed a globally increased relative theta (with and without photic stimulation) activity

T a b l e 1. Disorder Characteristics in the Examined Sampling

Т а б л и ц я 1. Характеристика розладів у обстеженій вибірці

Clinical Criteria		Migraine	Tension-type headache (TTH)
Headache type	pulsating	1	34
	squeezing	24	1
Associated with nausia and/or photophopia		22	2
Relieved with sleep and physical rest		20	29
Worsened by *	physical activity	17	7
	sleep deprivation or mental stress	6	22
Severity (affects ADL and forces a patient to stop activity)		24	4
Diurnal variation *		9	23
Positive family history for similar conditions		8	5
Duration of headache attack <6 hours *		20	14
Location of headache	all over the head and/or occipital	3	16
	frontal and/or temporal	22	19
Frequency (attack recurrence)	daily	1	8
	weekly	18	24
	monthly	6	3
Attacks are precipitated by:	physical exertion	10	6
	fasting and sleep deprivation	3	9
	Not specified	12	20

F o o t n o t e. * The difference between the two groups is statistically significant.

in migraineurs; this finding is in accordance with that of Lia et al. [27] who found a greater relative theta activity in the parieto-occipital region in adult migraineurs with and without aura. Neufeld et al. [28] reported that the peak alpha powers are lower in patients with classic migraine compared to controls. Genco et al. [31] also found that children suffering from migraine had increased theta activity compared to control subjects. Using interictal brain mapping, Seri et al. (47) were unable to find significant

T a b l e 2. Mean Values of the Powers of EEG Ranges in Migraine and Tension-Type Headache (TTH) Patients

Т а б л и ц я 2. Середні значення спектральних потужностей ЕЕГ-діапазонів у пацієнтів, що страждали на мігрень та головний біль, пов'язаний із напруженням

Leads		Groups, *P*	Spectral powers											
			Absolute, mV2/Hz			Relative, %			Absolute with photic stimulation			Relative with photic stimulation		
			delta	theta	alpha	delta	theta	alpha	delta	theta	alpha	Delta	theta	alpha
Frontal	F3	TTH	11.7	3.6	6.4	39.3	12.9	21.2	44.3	5.5	9.3	19.6	13.5	23.8
		migraine	20.6	7.4	6.4	58.9	26.6	18.1	60.3	9.3	4.9	20.6	24.1	14.3
		P value	0.108	0.037	0.73	<0.001	<0.001	0.418	0.79	0.251	0.063	<0.001	<0.001	<0.001
	F4	TTH	13.9	3.8	7.8	44.3	13.7	25.9	17.3	4.3	8.2	42.8	13.4	24
		migraine	22.1	8	6.4	58.1	24.5	15.7	32.2	16.6	13.4	55.7	23.9	14.8
		P value	0.267	0.418	0.277	<0.001	<0.001	0.005	0.35	0.267	0.45	<0.001	<0.001	<0.001
Central	C3	TTH	7.6	2.2	4.3	41	12.6	28.7	13.9	3.2	4.3	36.8	12.5	30.2
		migraine	9.8	5.3	5.7	45.3	22.8	26.1	14.4	15.4	5.7	43.2	25.1	21.2
		P value	0.194	0.083	0.828	0.134	<0.001	0.55	0.94	0.039	0.126	0.066	<0.001	0.004
	C4	TTH	8.6	2.6	5.3	38	13	30.7	11.5	3.8	10	37	13.7	30.4
		migraine	10.3	6.7	7.3	40	23	31.6	17.8	8.9	7.6	49.3	25.4	23.3
		P value	0.194	0.093	0.728	0.297	<0.001	0.822	0.685	0.037	0.946	<0.001	<0.001	0.104
Occipital	O1	TTH	33.5	9.6	43.2	36.8	10.1	37.8	31.6	14.5	50.1	30.4	10.7	225.1
		migraine	28.1	10.6	26.5	46.6	18.7	30.5	41	15.2	24.6	44.5	17.6	27.7
		P value	0.104	0.652	0.135	0.096	<0.001	0.17	0.857	0.916	0.09	0.015	0.006	0.002
	O2	TTH	8.3	2.7	7	43.8	12.4	27.9	14.2	4.9	9.4	39.4	14	26.8
		migraine	13.5	4.8	6.3	54.1	19.6	17.9	17.1	10.9	5.9	49.2	20.2	16
		P value	0.169	0.202	0.384	0.02	<0.001	0.006	0.642	0.073	o.254	0.007	<0.001	0.001
Parietal	P3	TTH	11.4	3.7	11	36.1	11.6	35.6	12.4	4	12.2	35.2	18.4	33.8
		migraine	16.9	6.8	13.1	45.7	22.3	27.1	26.2	12.4	12.5	44.8	22.1	22.4
		P value	0.337	0.041	0.426	0.009	<0.001	0.009	0.397	0.008	0.315	0.014	<0.001	<0.001
	P4	TTH	12.4	3.9	14.7	32.6	10	37.3	14.1	6.4	15.6	31.6	10.5	39.6
		migraine	15.9	7.7	14.2	41.8	18.5	30.2	25.8	14.9	12.1	40.3	23.3	24.9
		P value	0.33	0.113	0.392	0.004	<0.001	0.05	0.519	0.161	0.08	0.039	<0.001	<0.001
Temporal	T3	TTH	19.1	3.5	4.4	48.2	13.1	19.7	13.1	8.5	5	40.3	16.6	19.1
		migraine	17.1	6.7	5.8	51	21.4	17.2	21.4	9.2	5.6	50.8	23.1	15.6
		P value	0.115	0.132	0.636	0.236	<0.001	0.168	0.012	0.152	0.653	0.009	<0.001	0.152
	T4	TTH	12.8	3.2	5.1	39.3	12	21.9	13.3	4.6	6.1	41	13.7	19.9
		migraine	17.1	5.7	5.9	51.8	21.2	18.1	23.5	9.2	5.8	49.7	22	15.3
		P value	0.132	0.15	0.753	<0.001	<0.001	0.013	0.21	0.035	0.719	0.006	<0.001	0.02

F o o t n o t e s. *P* values are shown for between-group comparisons. Dashed blocks indicate cases of significant intergroup differences.

differences between migraineurs and controls. Interestingly, it was reported that background EEG activities of migraineurs and children suffering from epilepsy were significantly slower compared to those in healthy controls. No significant differences were found between migraineurs and epileptic patients [30]. Farkas et al. [48] described a higher central relative theta power in children with migraine.

The theta range is linked to the activity of hippocampal and thalamic networks during wakefulness and NREM sleep [49, 50]. Serotonergic impulsation from the dorsal raphe nucleus desynchronizes (suppresses) hippocampal theta waves under physiological conditions. So, a decrease in this serotonergic tone may augment theta activities [51]. Pathological theta waves may, on the one hand, represent slowing of the alpha rhythm related to reduced cerebral blood flow in the cortex. Intermittent frontotemporal theta oscillations are, on the other hand, usually attributed to disturbances in the deep midline structures [50]. Migraine was thought to be related to dysfunctional changes in the brainstem nuclei [52, 53]. Theta waves during wakefulness may indicate a number of pathophysiological conditions (including migraine), collectively known as "thalamic dysrhythmias" [54]. Calcium channels of the T and R types and calcium spikes may be involved in the generation of theta waves [55, 56]. Interestingly; there is certain evidence of cortical structural pathology in migraineurs. A reduced frontal grey matter density and diffusion abnormalities have been described in migraineurs, possibly explaining a longer response time during cognitive set-shifting [57–59]. Changes in the white and grey matter changes in migraine patients correlate with the severity of migraine [57, 60–62]. Repetitive activation of trigeminal vascular neurons may lead to neuronal cell damage in these areas mediated by intensified release of free radicals [63]. We did not find a significant linkage between the duration and frequency of migraine attacks and QEEG changes. This is in agreement with the results obtained by Bjørk et al. [64], as they did not find correlations between EEG slowing and the migraine attack frequency. Most of our migraine patients suffered from severe attacks; this was handicapping to study an effect of the attack severity on QEEG indices. However, Jonkman [65] did not find any correlation between EEG abnormalities and the migraine clinical severity.

We observed an increased relative delta activity in the frontal and parietal cortical areas of migraineurs. The delta activity is normally prevalent during deep sleep. It appears when the cholinergic impulsation from cortically projecting basal forebrain neurons decreases [50]. A pathological polymorphic delta activity can arise from both metabolic and structural pathologies in the underlying white matter or in the thalamus, hypothalamus, and midbrain reticular formation [50, 59].

Thus, our results demonstrate abnormal interictal cerebral functions that are more pronounced in migraineurs. This was possibly caused by activity changes in the subcortical and/or limbic structures. These abnormalities may be related to an underling genetic profile and pathology. The effect of migraine on the developing brain deserves obvious interest.

Informed consent was obtained from all participants; written consent was obtained from all patient parents. All procedures performed were in accordance with the ethical standards of the Helsinki declaration and were approved by the Department research board.

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ПОКАЗНИКИ ЕЕГ У ДІТЕЙ ІЗ ПЕРВИННИМИ РОЗЛАДАМИ, ПОВ'ЯЗАНИМИ З ГОЛОВНИМ БОЛЕМ

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Р е з ю м е

Епізодичні мігрень та головний біль, пов'язаний із напруженістю (tension-type headache – TTH), характеризуються сильними больовими нападами. Накопичуються вказівки на те, що функції головного мозку знаходяться поза нормою навіть у межах періодів між нападами. Ми намагались оцінити мозкові функції протягом інтеріктальних періодів у дітей із первинними проявами головного болю, використовуючи кількісний аналіз ЕЕГ. Були залучені 60 пацієнтів – 25 дітей, що страждали на мігрень, та 35 – із TTH; захворювання діагностували згідно з ICHD. У пацієнтів із мігренню у більшості ЕЕГ-відведень спостерігались істотно вищі, ніж у пацієнтів із TTH, нормовані спектральні потужності повільнохвильових діапазонів (тета та дельта) та зменшені значення нормованої потужності альфа-коливань. Окрім згаданих особливостей та негативної кореляції між віком та

потужностями дельта- і тета-коливань в обох обстежених групах, ми не змогли знайти будь-яких клінічних ознак, котрі б могли впливати на показники ЕЕГ. Наші результати свідчать на користь твердження, що мозкові дисфункції протягом інтеріктальних періодів є загалом більш типовими для пацієнтів із мігренню. Ці результати можуть допомогти краще забезпечувати захист мозкових функцій у дітей, що страждають на головний біль.

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